

## **I. Remarks**

Claims 9 and 10 are currently pending.

Claims 1, 4, 6-8, and 11 have been canceled without prejudice with this response.

## **II. Claim rejections under 35 U.S.C. § 103(a)**

A) Claims 1 and 11 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Snyder et al. (US 2002/0155580) taken with Simonet (U.S. Patent Serial No. 6,268,212). Applicants respectfully maintain that the Office has failed to provide an objective teaching or suggestion which would have motivated an artisan to combine the elements of the prior art to arrive at the specific combination of a B-domain deleted human Factor VIII protein operably linked to a liver specific promoter comprising a portion of the TTR gene promoter instantly claimed. Rather, the Office has combined the general teachings of Snyder regarding the utility of liver-specific promoters with Simonet's teaching regarding the utility of liver-specific promoters in developing transgenic mice to arrive at the instantly claimed invention. However, in the interest of furthering prosecution and without acceding to the correctness of the Office's rejection, Applicants have canceled claims 1 and 11 without prejudice. Withdrawal of the rejection is therefore requested.

B) Claims 1 and 6-8 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Snyder et al. (US 2002/0155580) taken with Simonet (U.S. Patent Serial No. 6,268,212) and further in view of Almstedt (WO 91/09122). In particular, the Office has concluded that it would have been obvious to a person of ordinary skill in the art to combine the teachings of Snyder and Simonet and Almstedt, a three way combination, to make a composition comprising a recombinant AAV comprising a nucleotide sequence encoding a B-domain deleted human Factor VIII protein, wherein said nucleotide sequence further encodes a junction that operably links said heavy and light chain of Factor VIII comprising SEQ ID NO: 15.

Applicants respectfully maintain that the Office has failed to provide an objective teaching or suggestion which would have motivated an artisan to combine the elements of the prior art to arrive at the specific combination of a B-domain deleted human Factor VIII protein operably linked to a liver specific promoter comprising a portion of the TTR gene promoter instantly claimed. Rather, the Office has combined the general teachings of Snyder regarding the utility of liver-specific promoters with Simonet's teaching regarding the utility of liver-specific promoters in developing transgenic mice to arrive at the

instantly claimed invention. However, in the interest of furthering prosecution and without acceding to the correctness of the Office's rejection, Applicants have canceled claims 1 and 6-8 without prejudice. Withdrawal of the rejection is therefore requested.

### **III. Claim rejections under the judicially created doctrine of obviousness-type double-patenting**

A) Claims 1 and 6-11 stand rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-25 of U.S. Patent No. 6,200,560. Claims 1, 4, 6-8, and 11 have been canceled without prejudice with this response. With respect to claims 9 and 10, Applicants have submitted with this response a terminal disclaimer that renders this rejection moot. In making this disclaimer, the Assignee of the instant application makes it with the understanding that this disclaimer serves the statutory function of removing the rejection of double patenting<sup>1</sup> and "raises neither presumption nor estoppel on the merits of the rejection"<sup>2</sup>. Accordingly, Applicants respectfully request its withdrawal.

B) A) Claims 1 and 6-11 stand rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-25 of U.S. Patent No. 6,221,349. Claims 1, 4, 6-8, and 11 have been canceled without prejudice with this response. With respect to claims 9 and 10, Applicants have submitted with this response a terminal disclaimer that renders this rejection moot. In making this disclaimer, the Assignee of the instant application makes it with the understanding that this disclaimer serves the statutory function of removing the rejection of double patenting<sup>3</sup> and "raises neither presumption nor estoppel on the merits of the rejection"<sup>4</sup>. Accordingly, Applicants respectfully request its withdrawal.

### **IV. Conclusion**

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

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<sup>1</sup> Quad Environmental Technologies Corp. v. Union Sanitary Dist., 946 F.2d 870, 874 (Fed. Cir. 1991)

<sup>2</sup> *Id.*

<sup>3</sup> Quad Environmental Technologies Corp. v. Union Sanitary Dist., 946 F.2d 870, 874 (Fed. Cir. 1991)

<sup>4</sup> *Id.*

Respectfully submitted,

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**V. Claim Amendments under 37 C.F.R. § 1.121**

1- 8. (Canceled)

9. (Previously presented)        A pharmaceutical composition comprising a recombinant adeno-associated virus (AAV) virion comprising a nucleotide sequence encoding a functional Factor VIII protein, wherein said recombinant adeno-associated virus virion lacks AAV rep and cap genes, wherein said Factor VIII protein is B domain-deleted , and wherein said nucleotide sequence comprises SEQ ID NO:13.

10. (Previously presented)        A pharmaceutical composition comprising a recombinant adeno-associated virus (AAV) virion comprising a nucleotide sequence encoding a functional Factor VIII protein, wherein said recombinant adeno-associated virus virion lacks AAV rep and cap genes, wherein said Factor VIII protein is B domain-deleted, and, wherein said nucleotide sequence comprises SEQ ID NO:14.

11. (Canceled)